

### **REMARKS**

In view of the following remarks, the Examiner is requested to allow Claims 1, 2, 4, 8, 11, and new Claims 36-38, the only claims pending and under examination in this application after entry of the above amendments.

Claim 1 has been amended to clarify the nature of the linker. Claims 27-29 have been cancelled. New Claims 36-38 have been added. Support for these amendments may be found throughout the specification and claims as originally filed. Specifically, support for the amendment to Claim 1 may be found at original Claim 7. Support for new Claim 36 may be found at page 11, lines 3 to 6, and support for new Claims 37 and 38 may be found at page 14, lines 17 to 21. Accordingly, no new matter has been added.

As no new matter has been added by way of this amendment, entry thereof by the Examiner is respectfully requested.

As an initial matter, the Applicants would like to thank the Examiner for acknowledging the patentability of Claim 11.

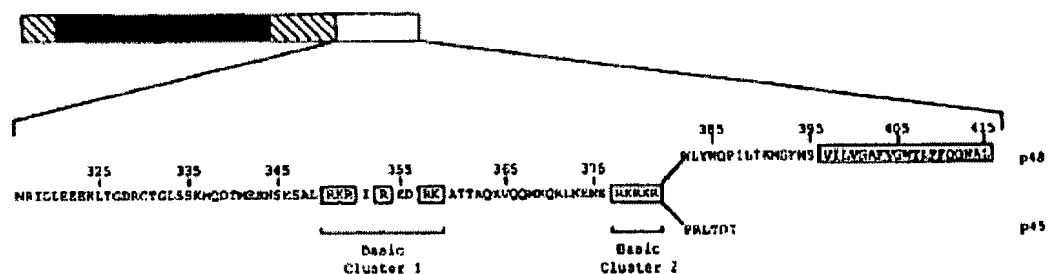
### ***Claim Rejections - 35 U.S.C. § 102***

Claims 1, 2 and 8 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Lorenzen, et al., Journal of Cell Biology, 1995, 131:631-643 ("Lorenzen").

According to the MPEP, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. See MPEP § 2131.

Claim 1 is directed to a composition. The composition includes a biologically active compound, a transport moiety and a linker moiety capable of self-immolation linking the biologically active compound and the transport moiety. Further, the transport moiety comprises a structure selected from the group consisting of  $(\text{ZYZ})_n\text{Z}$ ,  $(\text{ZY})_n\text{Z}$ ,  $(\text{ZYY})_n\text{Z}$  and  $(\text{ZYYY})_n\text{Z}$ , wherein each Z is L-arginine or D-arginine, and each Y is independently an amino acid that does not comprise an amidino or guanidino moiety, and wherein n is an integer of from 2 to 10. Accordingly, an element of the rejected claims is a self-immolating linker moiety.

The Office asserts that Lorenzen anticipates the Applicants' claimed invention because Lorenzen discloses the following construct:



Specifically, the Office asserts that in the above construct a catalytic region in black is equated with the Applicants' claimed biologically active moiety; a nuclear localization signal region, represented in part by the RKRKR basic cluster, is equated with the Applicants' claimed transport moiety; and an intervening sequence of amino acids is equated with the Applicants' claimed linker moiety.

The assertion of the Office fails however because the Office has mischaracterized the "intervening sequence" region as disclosed by Lorenzen. Specifically, the Office has not set forth where in the cited reference Lorenzen teaches that the referenced "intervening sequence" region performs the function of a linker moiety as that term is understood in the art and used in the context of the Applicants' disclosure. In fact, the "intervening sequence" region is simply not characterized by Lorenzen at all and hence the Office's characterization of that sequence of amino acids as a linker moiety is not supported by the teachings of

Lorenzen. If the Applicants are mistaken in this regard, the Office is invited to cite with particularity wherein Lorenzen characterizes the “intervening sequence” region as a “linker” region as that term is employed in the context of the Applicants’ specification. For this reason alone, this rejection may be withdrawn.

Additionally, even if the “intervening sequence” region could be interpreted as a linker moiety, Lorenzen still does not teach a “self-immolating” linker moiety. The Applicants raised this point in their previous response filed March 8, 2007, and yet the Office has failed to address this element of the claimed invention. Accordingly, once again the Applicants respectfully request that the Office either withdraw this rejection or set forth where in particularity Lorenzen teaches that the “intervening sequence” region, which the Office equates with the self-immolating linker moiety of the Applicants claims, is “self-immolating.”

According to the teachings of the Applicants’ specification, a “self-immolating” linker moiety is a moiety that may undergo autologous intermolecular cleavage, that is cleavage on its own. See, for instance, page 7, lines 1-5 and page 14, lines 17 to 21. The Applicants have reviewed Lorenzen and have not found where in the cited reference this element is taught.

In view of the above, the Applicants contend that Lorenzen does not teach all of the elements of the rejected claims, namely, a self-immolation linkage moiety. Consequently, because Lorenzen does not teach all the elements of the rejected claims it fails to anticipate the claimed invention. The Applicants, therefore, respectfully request that this rejection be withdrawn.

Claims 1 and 4 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Olsson et al., *Biochim. Biophys. Acta*, 1991, 1097:37-44 (“Olsson”).

As set forth above, an element of the rejected claims is a self-immolating linker moiety. According to the teachings of the Applicants’ specification, a “self-

immolating" linker moiety is a moiety that may undergo autologous intermolecular cleavage, that is cleavage on its own.

The Office asserts that Olsson anticipates the Applicants' claims because Olsson discloses a binding assay wherein the peptide fragment RSRSRSRSRSR was found to be capable of inhibiting the association of LDL and chondroitin 6-sulphate. Specifically, the Office asserts that the peptide fragment forms a complex with chondroitin 6-sulphate and that this complex anticipates the Applicants' claimed invention.

The assertion of the Office is deficient, however, because the Office has not set forth wherein Olsson teaches a linker moiety, let alone a "self-immolating" linker moiety. In fact, Olsson does not teach such a linker moiety because to the extent that the referenced peptide fragment inhibits the association of LDL and chondroitin 6-sulphate it is because the peptide fragment blocks the binding region responsible for the association. There is no teaching in Olsson that indicates that the interaction between the peptide and the chondroitin 6-sulphate involves an intermediary linker, rather the association is presumably direct. If the Applicants are mistaken in these regards, the Applicants invite the Office to point out with particularity specifically wherein Olsson discloses the necessity of a linker to facilitate the association of the peptide with the chondroitin 6-sulphate. For this reason alone, this rejection may be withdrawn.

Further, the Applicants would like to draw the attention of the Office to the fact that this was pointed out in the Applicants' last response filed on March 8, 2007, and yet the Office has failed to address this element of the claimed invention. For this reason alone, this rejection may be withdrawn.

Additionally, even if a linker moiety were disclosed in Olsson, there is still no teaching that such a linker moiety is a "self-immolating" linker moiety, as defined above. The Applicants have reviewed Olsson and have not found where in the cited reference this element is taught.

In view of the above, the Applicants contend that Olsson does not teach all of the elements of the rejected claims, namely, a self-immolation linkage moiety. Consequently, because Olsson does not teach all the elements of the rejected claims it fails to anticipate the claimed invention. The Applicants, therefore, respectfully request that this rejection be withdrawn.

Claims 1, 2, 4, and 8 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Mixson, US Patent No. 7,070,807 ("Mixson").

As set forth above, an element of the rejected claims is a self-immolating linker moiety. According to the teachings of the Applicants' specification, a "self-immolating" linker moiety is a moiety that may undergo autologous intermolecular cleavage, that is cleavage on its own.

The Office asserts that Mixson anticipates the Applicants' claims because Mixson discloses the use of a liposome for the intracellular delivery of a transport polymer that is in association with the transport polymer. Specifically, the Office asserts that Mixson discloses a polymer:liposome:DNA complex wherein the liposome functions as a linker linking the polymer and the DNA.

The assertion by the Office, however, is deficient because it is based on the erroneous assumption that the liposome actually links the polymer to the DNA. However, Mixson does not describe the liposome as "linking" the polymer to the DNA. Rather, Mixson merely indicates the components are mixed together and refers to that mixture as a complex without characterizing the nature of the referenced complex. In fact, it is unlikely that the liposome actually links the polymer to the DNA, as that term is used with reference to the Applicants' claims, because, as noted by the Office, Mixson discloses that the best transport efficiency was obtained by first mixing the transport polymer with the DNA and then mixing the resultant copolymer with the liposome. See Office Action, page 7. Thus, there is no indication that the mixing results in a complex wherein the liposome actually connects the transport polymer to the DNA. Hence, the assertion of the Office is

deficient because Mixson does not teach that the disclosed liposome is a linker. For this reason alone, this rejection may be withdrawn.

Additionally, even if the liposome disclosed by Mixson is considered a linker, there is still no teaching in Mixson that the liposome is "self-immolating." As the linker moiety as claimed is a "self-immolation linkage moiety," and Mixson fails to teach this element, Mixson does not anticipate the claimed invention. Accordingly, For this reason alone, this rejection may be withdrawn.

In view of the above, the Applicants contend that Olsson does not teach all of the elements of the rejected claims, namely, a self-immolation linkage moiety. Consequently, because Olsson does not teach all the elements of the rejected claims it fails to anticipate the claimed invention. The Applicants, therefore, respectfully request that this rejection be withdrawn.

### **New Claims**

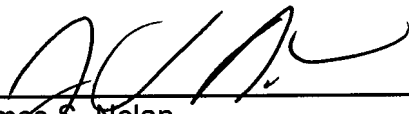
New Claims 36 to 38 depend from Claim 1. As set forth above, Claim 1 is patentable over the cited art. Accordingly, Claims 36 to 38 are also patentable.

**CONCLUSION**

In view of the amendments and remarks above, the Applicant(s) respectfully submit(s) that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

Respectfully submitted,

By:

  
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